

# Early alterations in adipose tissue biology and function in obese children

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## Rationale

- Expansion of fat mass can result from hypertrophy and/or hyperplasia.
- Accumulation of fat mass in obesity is associated with adipose tissue (AT) dysfunction in adults, particularly with inflammation.
- Clinical data indicate that obesity develops during early childhood.
- Along with increasing prevalence of obesity, related comorbidities such as insulin resistance and cardiovascular dysfunction emerge already in childhood.
- AT dysfunction is suspected to contribute to the clinical comorbidities.

## Objectives

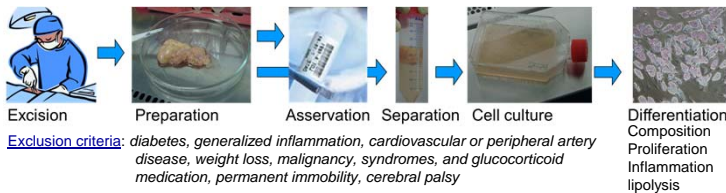
We hypothesize that AT dysfunction develops already in childhood and is related to clinical comorbidities in childhood obesity.

We aimed to evaluate obesity associated alterations in adipose tissue biology and function in lean and obese children.

- Composition (hypertrophy vs. hyperplasia)
- Function (differentiation, proliferation, lipolysis)
- Inflammation (macrophage infiltration)

## Research Design & Study Population

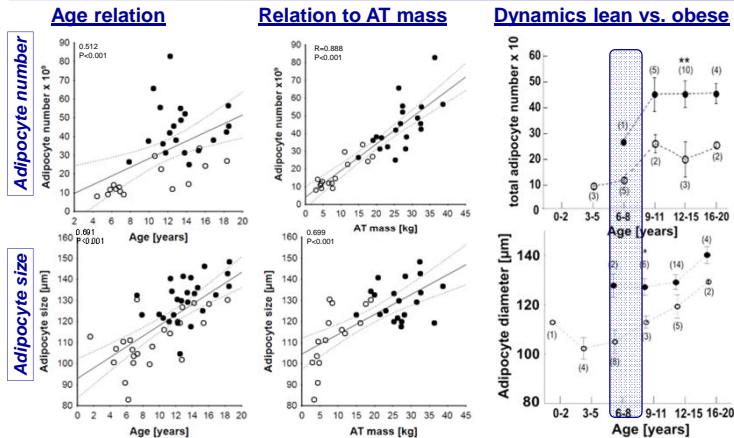
### Leipzig Childhood Adipose Tissue Bank



	Lean (n=106)		Obese (n=65)		p
	Mean±SEM	Range	Mean±SEM	Range	
Male/Female (% ♂)	67/39 (63.2)		37/28 (56.9)		0.414
Age [years]	7.6±0.6	0.1–18.4	11.4±0.6	1.0–18.4	<0.001
BMI SDS	-0.34±0.09	-2.53–1.24	2.29±0.07	1.32–4.17	<0.001
Skinfold [mm]	14.8±0.8	5.0–27.0	28.0±1.0	11.1–40.8	<0.001
Waist circumf. [cm]	58.7±1.2	40–83	91.2±2.4	51–154	<0.001
AT mass per kg	9.8±1.0	2.1–23.9	26.4±1.4	4.6–60	<0.001

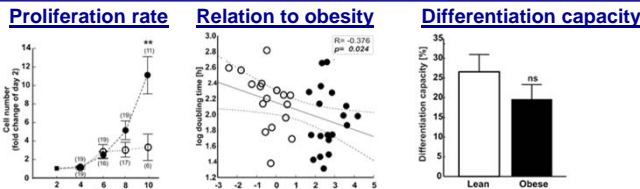
## Results

### 1. Hypertrophy and hyperplasia of AT in obese children



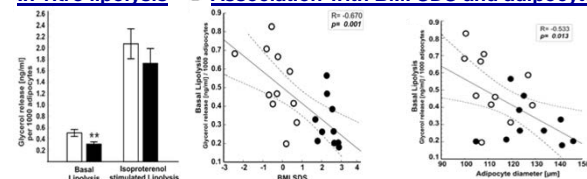
Adipocyte number is >2fold increased in obese children, related to fat mass. Adipocyte size is 17% larger in obese children, closely related to fat mass. AT of obese children shows hyperplasia and hypertrophy from early age on.

### 2. Functional alterations in AT of obese children



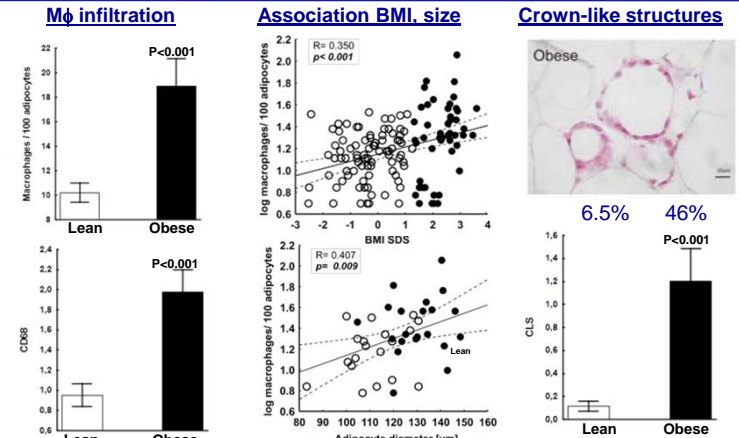
No differences in number of obtained SVF cells or % adherent cells. Proliferation was not related to age or adipocyte size. No differences in differentiation rate between lean and obese children. Nonreduced proliferation may underlie AT hyperplasia in obese children.

### In vitro lipolysis Association with BMI SDS and adipocyte size



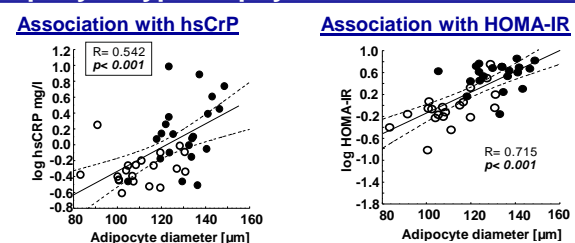
Normal response of adipocytes of lean and obese children to betaadrenergic stimulation of lipolysis, but decreased basal lipolysis in obese children. Reduced basal lipolysis may contribute to adipocyte hypertrophy in obesity.

### 3. Macrophage infiltration in AT of obese children



Mφ infiltration in AT is doubled in obese children and is majorly related to cell size. Formation of CLS occurs in almost 50% of obese children.

### 4. Adipocyte hypertrophy is related to insulin resistance



Inflammatory markers and insulin resistance markers are closely and independently related to larger adipocyte size.

## Conclusions

- Adipocyte size and number increase with normal childhood development.
  - Obese children already show adipocyte hypertrophy and hyperplasia.
  - Increased proliferation and decreased basal lipolysis may contribute to the hyperplasia and hypertrophy, respectively.
  - AT hypertrophy is associated with macrophage infiltration in obese children indicating enhanced AT inflammation starting at preschool age.
  - Adipocyte hypertrophy is directly related to signs of insulin resistance.
- Evidence for AT dysfunction in obese children in already early childhood.**